Remarks

Claims 4, 5, 8-12, 26, 27, 30, and 32 have been withdrawn as directed to a non-elected invention. In accordance with M.P.E.P. § 809 and as noted in the Office Action dated October 4, 2004, these claims will be examined upon the allowance of the linking claims, i.e. claims 1, 2, 14-28, and 31. Therefore, the withdrawn claims are still pending and amended, as appropriate.

In particular, claim 4 was amended to depend from claim 1, and to specify that the agent is delivered in a polymer. Support for this amendment can be found in the specification at least at page 8, lines 22-24. Claim 5 has been canceled. Claim 10 was amended to correct a grammatical error. Claim 12 was amended to depend from claim 1.

Amendments to the Specification

Pages 3 and 4 have been amended to correct typographical errors. Pages 25 and 26 have been amended to include the complete name for the growth factors that were listed using abbreviations. No new matter was added.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-3, 6, 7, and 13-15 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection.

The Legal Standard

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art,

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without undue experimentation (*See, e.g., Amgen v. Hoechst Marion Roussell,* 314 F.3d 1313 (Fed. Cir. 2003; *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (*M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985)).

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir.1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." *Atlas Powder Co., v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir.1984). There is no requirement for examples.

The claims are enabled

The specification teaches one of ordinary skill in the art how to make and use the claimed methods, kits, and devices without undue experimentation. The amended claims define a method

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for treating an organ, organ component, or tissue structure by delivering a therapeutic agent or system to the endomural zone of the organ, organ component, or tissue structure and devices and kits for practicing this method. The state of the art is well-established. Surgical methods, percutaneous administration and similar procedures have been practiced for many years. The endomural zone is well-defined in the specification and well-known in the art (see e.g. page 6, lines 1-28). In fact, in her rejection, the Examiner accurately characterized the endomural zone of the heart as the myocardium. The specification provides many examples of organs, organ components, and tissues to be treated (see e.g. page 4, lines 21-26, regarding the myocardium of the heart; page 5, lines 19-26, listing organs and organ components; and page 6, lines 1-30, discussing the location of the endomural zone), and suitable methods and devices with which to treat the endomural zones of these organs, organ components, and tissues (see e.g. page 9, line 1 until page10, line 19 and Figures 3-5). Therefore one of ordinary skill in the art would know how to make and use the claimed method and device without undue experimentation.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-3, 6, 7, 13-25, 28, 29, 31, and 33 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the

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specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). The fact that other language may be used in a claim is not a valid basis for a rejection under 35 U.S.C. § 112, second paragraph. The M.P.E.P. explains that the examiner's focus during examination of claims for compliance with the definiteness requirement "is whether the claim meets the threshold requirements of clarity and precision, *not whether more suitable language or modes of expression are available.*" (M.P.E.P. 2173.02, emphasis added)

The Claims are Definite

Claim 1

Claim 1 was has been amended to recite two steps for the method:

(a) penetrating and entering the endomural zone of an organ, organ component or tissue structure with a means for delivery of a therapeutic, prophylactic or diagnostic agent, and

(b) delivering the therapeutic, prophylactic or diagnostic agent to the endomural zone in a form for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent to the endomural zone, where the agent is delivered in a carrier selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, microparticles and microcapsules, nanoparticles and combinations thereof.

Support for these amendments can be found in the specification at least page 5, lines 5-12; page 7, lines 5-15; and claim 5 as originally filed.

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The phrase "locally penetrating" has been deleted from claim 1. However, "locally" is a well-known term in the art. Stedman's Medical Dictionary defines "local" as "having reference or confined to a limited part; not general or systemic" and "localization" as "limitation to a definite area". (see attached copies from Stedman's Concise Medical Dictionary (Third Ed.) (1987)) Additionally, the specification describes "localized treatment" and "local therapy" at page 7, lines 5-29, as a method which "[focuses] treatment of the endomural region of an organ or tissue [...], while sparing exposure to surrounding contiguous or adjacent healthy tissue." Therefore the term "local" is definite. Therefore claim 1 as amended is definite.

Claim 2

Claim 2 has been canceled and incorporated into claim 1.

Claim 13

Claim 13 has been amended to correct antecedent basis.

Claims 15 and 25

The phrase "end penetrating or cutting means" has been deleted from claims 15 and 25, and replaced with "means for creating a void that is larger than the device". Support for this amendment can be found in the specification at least at page 11, line 23 until page 12, line 2. However, the phrase "end penetrating or cutting means" is definite. One of ordinary skill in the art knows that devices must contain an end. The specification describes a number of penetrating and cutting means that are designed to cause minimal collateral damage to tissue surrounding the site where a void is created (*see e.g.* page 9, lines 1-19; and Figures 3-5). Claims 15 and 25 have

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also been amended to specify that the device includes "means for local delivery of therapeutic, prophylactic or diagnostic agents". Support for this amendment can be found in the specification at least at page 7, lines 10-15 and page 11, line 10. A number of "means for delivery of agents" are disclosed in the specification. For example, page 10, lines 3-4 describes administering drug by force through an actuator means that propels drug particles through a macroporous membrane (*see also* Figure 4A); page 10, lines 12-15 describes administering drug via a piezoelectric pump (*see also* Figure 5A); page 10, line 20 describes percutaneous administration of drugs; and page 30, lines 23-24 and 28-30 discloses using catheters, syringes, sprays, trocars, or scopes to administer therapeutic systems. Therefore claims 15 and 25, as amended, are definite.

Claim 17

Claim 17 has been amended to delete "catheter-like device" and replace it with "tubular tissue accessing device". Support for this amendment can be found in the specification at least at page 4, lines 18-19. Therefore claim 17, as amended is definite.

Claim 19

Claim 19 has been amended to replace "tissue space" with "void." Support for this amendment can be found in the specification at least at page 11, line 22. Claim 19 has been further amended to delete "distal" and specify that expansile cutter is located an end of the hollow tubular member. Therefore claim 19, as amended, is definite.

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Claim 31

One of ordinary skill in the art would know the types of devices that are suitable for use in nerve regeneration. For example, page 26 of the specification discusses types of techniques that can be used for nerve regeneration (see page 26, lines 14-19). Therefore claim 31 is definite.

Rejection Under 35 U.S.C. § 102

Claims 1-3, 6, 7, 15-18, 20-23, 25, 28, and 29 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,585,716 to Altman ("Altman '716"). Claims 1-3, 6, 7, 15-18, 20-23, 25, 28, and 29 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,102,887 to Altman ("Altman '887"). Claims 1-3, 6, 14-16, 18, 20-25, 28, and 29 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,309,370 to Haim *et al.* ("Haim"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Altman '716

Altman '716 describes methods for treating the human heart. A guide catheter is placed in the venous portion of a patient's vasculature and extends until the vena cava and coronary sinus. A drug delivery catheter is inserted inside the guide catheter and extends beyond the guide catheter so that the tip enters the cardiac vein and extends to the posterior vein. The tip contains a penetrating element, such as a curved or helical needle, that is selectively extended into the wall of the vein and into the myocardium. Therapeutic agents are injected into the myocardium, through the needle (col. 4, lines 5-19 and Figure 1). The guide catheter contains an

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occluding mechanism. The venous flow path is shut off by occluding the oronary ostium with the occluding mechanism. This stops the natural blood flow from the myocardium into the vein, thereby preventing the therapeutic agents from being flushed out of the myocardium in the course of normal blood flow. (col. 4, lines 20-47)

Altman '716 does not disclose every step of the claimed method. Altman '716 does not describe delivering the therapeutic agent locally to the endomural zone, wherein the therapeutic agent is in a form suitable for local delivery. Altman '716 requires an occlusion step to prevent the delivery of the drug beyond the site of administration. Thus, Altman 716's does not describe a therapeutic agent that is in a form for local delivery. Therefore claim 1, and its dependent claims, claims 2, 3, 6, and 7 are novel over Altman '716.

Altman '716 does not disclose every element of the claimed kit. Claim 25 has been amended to specify that the void filling material or implant is in a form suitable for local administration. Support for this amendment can be found in the specification at least at page 7, lines 5-18. Although Altman '716 mentions that controlled release systems can be administered, it does not disclose administering such systems in a form suitable for local administration. These controlled release systems effect systemic delivery. Altman' 716 states that its method, which involves administration through the venous side of the heart, is particularly useful for avoiding embolic events because "even if a large portion of the injected microspheres wash out of the delivery site during and after injection [...], there would be little chance of embolic events". Thus, Altman '716 discloses that its systems are easily removed from the site of administration.

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As noted above, Altman '716 requires the step of occluding the oronary ostium to decrease the rate of removal of the therapeutic agents from the myocardium. Therefore, claim 25, and its dependant claims, claims 28 and 29, are novel over Altman '716.

Altman '716 does not disclose the claimed devices. Altman '716 uses a needle to enter the tissue space and administer a therapeutic agent. It does not disclose a device with means for creating a void, as required by claim 15 as amended. Therefore claim 15, and its dependent claims, claims 16-18 and 20-23, are novel over Altman '716.

Altman '887

Altman '887 describes a steerable catheter with a deployable penetrating element, such as a helical or straight needle, for administration of drugs to the heart (col. 3, lines 9-22). Col. 9, lines 20-52 discloses an expanding prong fixation system, which may be used to stabilize the needle. Altman '877 does not disclose every step of the claimed method. As noted above, regarding Altman '716, in the course of normal blood flow, therapeutic agents can be removed from the site of administration. Although Altman '877 uses the term "local delivery" in the specification (see e.g. col. 1, lines 5-6 and 11-12), it does not disclose delivering a therapeutic agent in a form suitable for local delivery. Therefore claim 1, and its dependent claims, claims 2, 3, 6, and 7, are novel over Altman '877. Similarly, claim 25 and its dependant claims, claims 28 and 29, are novel over Altman '877.

Like Altman '716, Altman '877 uses a needle to administer a therapeutic agent. It does not disclose a device with means for creating a void, as required by claim 15 as amended.

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Therefore claim 15, and its dependent claims, claims 16-18 and 20-23, are novel over Altman '877.

Haim

Haim discloses a method and device for delivery of growth factors to an ischemic region in the heart. Haim emphasizes the importance of navigating the catheter to the site of the ischemic regions (see col. 4, lines 25-40). The device is a catheter that contains sensors to determine the position of the catheter with respect to the heart wall (col. 12, lines 10-28). When the device is in place, the needle is placed inside the heart wall and the growth factors are delivered (see e.g. col. 12, lines 40-49 and col. 13, lines 39-50 and col. 14, lines 3-11). The growth factors may be administered in a solution or a capsule (see col. 15, lines 14-20). . Haim does not disclose administering agents in a carrier such as porous matrices, hydrogels, organogels, colloidal suspensions, microparticles, microcapsules, or nanoparticles. Therefore claim 1 and its dependent claims, claims 2, 3, 6, and 7, are novel over Haim.

Haim does not disclose means for creating a void. Haim merely penetrates the heart wall and administers a therapeutic using a needle. Therefore claim15, and its dependent claims, claims 16-18 and 20-23, are novel over Altman '877.

Haim does not disclose including a void filling material or implant in the drug delivery device. Haim administers a drug in the form of a solid polymeric matrix capsule (see col. 15, lines 14-20). In the preferred embodiment, the capsule is designed to disintegrate. Therefore claim 25 and its dependent claims, claims 28 and 29, are novel in view of Haim.

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Rejection Under 35 U.S.C. § 103

Claims 13 and 33 were rejected under 35 U.S.C. § 103(a) as being obvious over Altman '716, Altman '887, or Haim, in view of Benjamin & McMillan, *Circ. Res.*, 83: 117-132 (1998) ("Benjamin"). Claim 31 was rejected under 35 U.S.C. § 103(a) as being obvious over Brösamle, et al., *J. Neuroscience*, 20(21):8061-8068 (2000) ("Brösamle"), in view of Altman '716, Altman '887, or Haim. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claims 13 and 33

Claim 13 is a method claim that depends from claim 3 and further defines the therapeutic agent as a heat shock proteins, stress response proteins, or inducers of heat shock or stress response proteins. Claim 33 is a kit claim that depends from claim 25 and further defines the kit as containing stress response inducing agents or stress response proteins.

The combination of Altman '716, Altman '887, or Haim with Benjamin

As noted above, Altman '716 does not disclose the local administration of therapeutic agents or systems. Altman '887 does not disclose the local administration of therapeutic agents or systems. Haim does not disclose local administration of an agent in a carrier, such as porous matrices, hydrogels, organogels, colloidal suspensions, microparticles or microcapsules, or nanoparticles. Additionally Haim does not disclose including a void filling material or implant in the device. Benjamin is a general reference about heat shock proteins and some of their roles. Benjamin does not cure the deficiencies of Altman '716, Altman '887, and Haim. The

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combination of these references still does not disclose or suggest delivering heat shock proteins, stress response proteins, and inducers of heat shock or stress response proteins in a form suitable for local administration as defined by claim 13. Additionally, the combination of Benjamin with Altman '716, Altman '887, and Haim does not disclose a kit containing a void filling material or implant is in a form suitable for local administration, as required by claim 33.

Claim 31

Claim 31 is device claim that depends from claim 15 and further defines the device as being suitable for nerve regeneration.

The combination of Brösamle with Altman '716, Altman '887, or Haim

As noted above, Altman '716, Altman '887 and Haim are limited to devices that use needles to penetrate a tissue and administer a therapeutic agent. None of these references disclose a device that is able to create a void. Brösamle describes administering an antibody to the spinal cord to promote regeneration. Brösamle does not cure the deficiencies Altman '716, Altman '887 and Haim. Brösamle does not disclose a device with means for means for creating a void. Therefore the combination of Brösamle with Altman '716, Altman '887, or Haim does not make claim 31 obvious.

Objections to the Claims

Claims 2, 3, 7, 14-16, and 25 were objected to for informalities.

Claims 2, 3, 14, 15, and 25 were objected to for containing non-elected subject matter. Applicants respectfully traverse this objection. As noted above, and as noted in the Office

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Action dated October 4, 2004, the non-elected subject matter will be examined upon the allowance of the elected subject matter. Therefore, the portions of claims 2, 3, 14, 15, ad 25 which contain non-elected subject matter have not been deleted.

Claim 7 was objected to for containing abbreviations. In response, claim 7 has been amended to contain the complete name for each growth factor listed therein.

Claim 16 was objected to for missing a word. In response, claim 16 has been amended to insert the word "and" between "rigid" and "made".

Additional Amendments to the claims

Claims 3, 10 and 12 were amended to correct antecedent basis. Claim 14 was amended to clarify the order of the steps and to delete the depositing step. Claim 24 was amended to provide the complete name for each abbreviation.

New claims 34-37 have been added. New claim 34 depends from claim 14 and contains the depositing step in former claim 14. New claim 35 depends from claim 1 and specifies that the organ, organ component, or tissue structure is accessed percutaneously, surgically, or via endoluminal entry. Support for this claim can be found in the specification at least at page 9, lines 1-8. New claims 36 and 37 further define the drug delivery means of claim 1. Support for these claims can be found in the specification at least at page 4, lines 18-19.

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Allowance of claims 1, 3, 4, and 6- 37, as amended, is respectfully solicited.

Respectfully submitted,

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